

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference LEA36520-WO	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/EP2004/004455	International filing date (day/month/year) 28.04.2004	Priority date (day/month/year) 09.05.2003
International Patent Classification (IPC) or national classification and IPC		
Applicant BAYER HEALTHCARE AG		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of **10** sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

a. ☐ (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:

☐ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

b. ☐ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

<input checked="" type="checkbox"/>	Box No. I	Basis of the report
<input type="checkbox"/>	Box No. II	Priority
<input checked="" type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
<input type="checkbox"/>	Box No. IV	Lack of unity of invention
<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
<input checked="" type="checkbox"/>	Box No. VI	Certain documents cited
<input type="checkbox"/>	Box No. VII	Certain defects in the international application
<input checked="" type="checkbox"/>	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

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Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____ which is the language of a translation furnished for the purposes of:

- ☐ international search (Rule 12.3 and 23.1(b))
☐ publication of the international application (Rule 12.4)
☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:

pages 1-78 as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ the claims:

nos. 1-14 as originally filed/furnished

nos.* _____ as amended (together with any statement) under Article 19

nos.* _____ received by this Authority on _____

nos.* _____ received by this Authority on _____

☐ the drawings:

sheets _____ as originally filed/furnished

sheets* _____ received by this Authority on _____

sheets* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing (*specify*): _____

☐ any table(s) related to sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing (*specify*): _____

☐ any table(s) related to sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

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Box No. III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 13-14

because:

☒ the said international application, or the said claims Nos. 13-14

relate to the following subject matter which does not require an international preliminary examination (*specify*):

Claims 13 and 14 relate to subject matter which, in the opinion of this Authority, falls under PCT Rule 67.1(iv). Consequently, no expert opinion has been established in respect of the industrial applicability of the subject matter of said claims (PCT Article 34(4)(a)(i)).

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____ are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _____

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

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Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement		
1. Statement			
Novelty (N)	Claims	7-14	YES
	Claims	1-6	NO
Inventive step (IS)	Claims	7-14	YES
	Claims	1-6	NO
Industrial applicability (IA)	Claims	1-12	YES
	Claims		NO
2. Citations and explanations (Rule 70.7)			
1) This report makes reference to the following documents:			
D1: WO 03/093269 A			
D2: WO 02/09713 A			
D3: CH 396 925 A			
D4: REDDY, K. HEMENDER ET AL: "Versatile synthesis of 6-alkyl(aryl)-1 H-pyrazolo[3,4-d]pyrimidin-4[5H]-ones" INDIAN JOURNAL OF CHEMISTRY, SECTION B: ORGANIC CHEMISTRY INCLUDING MEDICINAL CHEMISTRY, 31 B(3), 163-6 CODEN: IJSBDB; ISSN: 0376-4699, 1992, XP009034712			
D5: MIYASHITA, AKIRA ET AL: "Studies on pyrazolo[3,4-d]pyrimidine derivatives. XVIII. Facile preparation of 1 H-pyrazolo[3(4-d]pyrimidin-4(5H)-ones" HETEROCYCLES, 31 (7), 1309-14 CODEN: HTCYAM; ISSN: 0385-5414, 1990, XP002953484			
D6: CHENG, C. C. ET AL: "Potential purine antagonists. VII. Synthesis of 6-alkylpyrazolo[3,4-d]pyrimidines" JOURNAL OF ORGANIC CHEMISTRY, 23, 191-200 CODEN: JOCEAH;			

Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement

ISSN: 0022-3263, 1958, XP002293718

2) Novelty

D2 pertains to the use of PDE 2 inhibitors of the general formula (I) (see page 4), which differ from the present compounds by the substituents in positions 1 and 6.

D3 describes a process for preparing pyrazolo[3,4-d]pyrimidines. The present formula (I) can be considered to be a selection of specific substituents (that is, a hydrogen atom in position 3 and a CH₂ group in position 6) from the range described in D3. However, D3 does not explicitly disclose a compound that falls under the general formula in the present claim 1.

Some compounds described in D4-D6 overlap with the present formula (I), as shown below:

- D4: page 465, compounds 4u, 4v, 4e and 4x;
- D5: page 1310, compounds 1c, 1d and 1e;
- D6: page 195, table II (17 compounds).

In light of the disclosure of D4-D6, the present claims 1-6 do not meet the requirements of PCT Article 33(2).

Conversely, the subject matter of claims 7-14 is novel within the meaning of PCT Article 33(2).

Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**3) Inventive step**

Since some of the claims do not meet the requirements of PCT Article 33(2), a definitive conclusion cannot be reached with respect to the inventive step of the claimed subject matter.

However, the following points should be taken into consideration:

D2, which is considered to represent the prior art closest to the subject matter of claims 7-14, discloses selective PDE 2 inhibitors as drugs for improving cognition, the ability to concentrate, learning ability and/or memory.

Compounds of the present formula (I) differ from those indicated in D2 by the substituents in positions 1 and 6.

The problem addressed by the present invention may therefore be considered that of providing further compounds for improving cognition, the ability to concentrate, learning ability and/or memory.

The applicant has shown by several examples (see page 20, table 1) that pyrazolopyrimidine derivatives of the present formula (I) solve the above-indicated technical problem.

Since the closest prior art contains no suggestion that would lead a person skilled in the art to

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prepare pyrazolopyrimidines substituted in position 6 by cyclylmethyl or alkylmethyl and in position 1 by phenyl or heteroaryl, the subject matter of the present claims 7-14 satisfies the criteria of PCT Article 33(3).

4) Industrial applicability

The PCT Contracting States do not have uniform criteria for assessing the industrial applicability of claims 13-14 in their present form. Patentability may also depend on the wording of the claims. The EPO, for example, does not recognize the industrial applicability of claims to the medical use of a compound; it may, however, allow claims to the first medical application of a known compound or to the use of such a compound in the manufacture of a drug for a new medical application.

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Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

Application No.
Patent No.

Publication date
(day/month/year)

Filing date
(day/month/year)

Priority date (valid claim)
(day/month/year)

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure

Date of non-written disclosure
(day/month/year)

Date of written disclosure
referring to non-written disclosure
(day/month/year)

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Clarity

Prodrug: the applicant states (description, page 5, lines 24-27) that the present invention also comprises prodrugs of the compounds according to the invention.

Although the description gives details clarifying the meaning of this term, the structure of a prodrug cannot be precisely defined (PCT Article 6).

Since it is not possible for a person skilled in the art to establish which compounds fall within the definition of a prodrug, this term should be deleted.

The novelty and inventive step of prodrugs of the present compounds have not been examined.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

Box VI**Provisional literature**

The present international preliminary examination does not refer to the content of D1 (international publication date: 13 November 2003). However, D1 could become relevant to the evaluation of novelty on entering the regional phase.